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September 27, 1996

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Attention: TSCA 8(e) Coordinator
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street S. W.
Washington, DC 20460

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Supplemental TSCA 8(e) Information for Tertiary Amyl Methyl Ether (TAME)

Dear Sir or Madam:

This information is submitted as supplement to a previous TSCA 8(e) notification filed on behalf of Amerada Hess Corporation, Chevron Products Company, CITGO Petroleum, Exxon Company USA, Marathon Oil Company, Sun Refining and Marketing, and Texaco Refining and Marketing. This information is based on test results obtained under the Enforceable Consent Agreement (54 FR 14910 - March 21, 1995) for TAME (CAS No. 994-05-8). The required studies are being coordinated by staff from the American Petroleum Institute.

On April 12, 1996, a TSCA 8(e) letter was submitted to EPA describing results from a range-finding study for developmental toxicity in mice and rats (copy attached). In that study, an increased incidence of cleft palate was found in the pups of pregnant mice exposed to 4000 ppm TAME. Results from the definitive study in rats and mice are now available.

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In the definitive study in mice;

- At 3500 ppm, TAME caused maternal toxicity including mortality (four of 25), reduced body weight, increased liver weight, and treatment-related clinical signs of central nervous system depression (ataxia, gasping, rough coat, lethargy, eyes squinted, head tremors and slow respiration). Developmental toxicity included increased incidence of late fetal deaths, reduced fetal body weights per litter, increased incidence of cleft palate (eleven fetuses in six litters), and enlarged lateral ventricles of the cerebrum.
- At 1500 ppm TAME, dams displayed increased liver weight and limited clinical signs of central nervous system depression including eyes half closed and head tremors (one dam each). Developmental toxicity was limited to an increased incidence of cleft palate (three fetuses in three litters).

- At 250 ppm TAME, no maternal or fetal toxicity was observed. In the previous range-finding study, the no-observed-adverse-effect-level was determined to be 1000 ppm TAME.

The observations of cleft palate in fetuses at 1500 and 3500 ppm TAME is consistent with the proposed mechanism for cleft palate in mice exposed to a variety of stressful physical and chemical agents (see our April 12, 1996 letter). We believe that exposure to anesthetic concentrations of TAME caused maternal stress which in-turn caused cleft palate in the developing mice.

As expected, rats exposed to TAME did not have any findings of cleft palate in the range-finding study or this definitive study. In the rat definitive study, the maternal NOAEL was 250 ppm and the developmental NOAEL was 1500 ppm.

The final report for this study will be forwarded to EPA under the conditions of the Enforceable Consent Agreement, Docket Number OPPTS-4205Q. If you have any questions about this information, please contact Dr. Richard Rhoden at the American Petroleum Institute (202) 682-8480.

Sincerely,

RD Cavalli/RDW

Richard D. Cavalli
Manager, Toxicology & Health Risk Assessment

Enclosure: 1

cc. Mr. Gary Timm
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